

**AIR MAIL**

JC04 Rec'd PCT/PTO - 1 AUG 2005

PTO-1390 (Rev. 02-2005)

Approved for use through 3/31/2007. OMB 0651-0021  
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371</b>		<b>ATTORNEY'S DOCKET NUMBER</b> <b>3244-98</b>
INTERNATIONAL APPLICATION NO. PCT/CA2004/000151	INTERNATIONAL FILING DATE February 4, 2004	U.S. APPLICATION NO. (If known, see 37 CFR 1.5) <b>10/544175</b>
TITLE OF INVENTION METHOD OF INHIBITING DIHYDROFOLATE REDUCTASE; SCREENING ASSAY FOR THE IDENTIFICATION OF NOVEL...		
APPLICANT(S) FOR DO/EO/US Eric D. BROWN; Xiaoming LI; Gerard WRIGHT; Jonathan D. CECHETTO; Michela JURAN; Rebecca HARTLEN		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"> <li>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a submission under 35 U.S.C. 371.</li> <li>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a submission under 35 U.S.C. 371.</li> <li>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</li> <li>4. <input checked="" type="checkbox"/> The US has been elected (Article 31).</li> <li>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))             <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input checked="" type="checkbox"/> has been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ol> </li> <li>6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).             <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto.</li> <li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li> </ol> </li> <li>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))             <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input checked="" type="checkbox"/> have not been made and will not be made.</li> </ol> </li> <li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</li> <li>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</li> <li>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</li> </ol>		
<b>Items 11 to 20 below concern document(s) or information included:</b>		
<ol style="list-style-type: none"> <li>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li> <li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li>13. <input checked="" type="checkbox"/> A preliminary amendment.</li> <li>14. <input checked="" type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li> <li>15. <input type="checkbox"/> A substitute specification.</li> <li>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</li> <li>17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821- 1.825.</li> <li>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).</li> <li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li> <li>20. <input type="checkbox"/> Other items or information:</li> </ol>		

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

U.S. APPLICATION NO. (if known, see 37 CFR 1.6) <b>10/544175</b>		INTERNATIONAL APPLICATION NO. PCT/CA2004/000151		ATTORNEY'S DOCKET NUMBER 3244-98	
The following fees are submitted: 21. <input checked="" type="checkbox"/> Basic national ..... \$300 <b>\$ 300.00</b> 22. <input checked="" type="checkbox"/> Examination Fee If international preliminary examination report prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4) ..... \$100 All other situations ..... \$200 23. <input checked="" type="checkbox"/> Search fee Search fee (37 CFR 1.445(a)(2) has been paid on the international application to the USPTO as an International Searching Authority ..... \$100 International Search Report prepared and provided in the Office ..... \$400 All other situations ..... \$500					
<b>TOTAL OF 21, 22 and 23 =</b> <b>\$ 1000</b>					
<input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.					
Total Sheets	Extra sheets	Number of each additional 50 or fraction thereof (round up to a whole number)		RATE	
- 100 =	0/50 =			x \$250	<b>\$ 0</b>
Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)).					
CLAIMS		NUMBER FILED	NUMBER EXTRA	RATE	\$
Total claims		- 20 =	0	x \$50	<b>\$ 0</b>
Independent claims		- 3 =	0	x \$200	<b>\$ 0</b>
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+ \$360	<b>\$ 0</b>
<b>TOTAL OF ABOVE CALCULATIONS =</b> <b>\$ 1000</b>					
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by ½.					
<b>SUBTOTAL =</b> <b>\$ 500.00</b>					
Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)).					
<b>TOTAL NATIONAL FEE =</b> <b>\$ 500.00</b>					
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property					
<b>TOTAL FEES ENCLOSED =</b> <b>\$ 500.00</b>					
Amount to be refunded: _____ Amount to be charged: _____					
a. <input checked="" type="checkbox"/> A check in the amount of \$ <u>500.00</u> to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>02-2095</u> . A duplicate copy of this sheet is enclosed. d. <input type="checkbox"/> Fees are to be charged to a credit card. <b>WARNING:</b> Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.					
NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.					
SEND ALL CORRESPONDENCE TO: Bereskin & Parr Box 401, 40 King Street West Toronto, Ontario M5H 3Y2					
SIGNATURE <u>Patricia Power</u> NAME <u>51,379</u> REGISTRATION NUMBER					

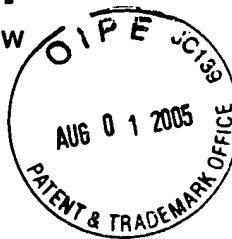
10/544175

JC04 Res'd PCT/PTO - 1 AUG 2005

# Bereskin & Parr

INTELLECTUAL PROPERTY LAW

July 29, 2005



Patricia Power B.Sc., Ph.D. (Chem)  
416 957 1683 pfolkins@bereskinparr.com

Your Reference: PCT/CA2004/000151  
Our Reference: 3244-98

The Commissioner of Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Transmitted herewith for entry into national phase of the patent application of

Inventors: Eric D. BROWN et al.

For: **METHOD OF INHIBITING DIHYDROFOLATE REDUCTASE; SCREENING ASSAY FOR THE IDENTIFICATION OF NOVEL THERAPEUTICS AND THEIR CELLULAR TARGETS**

The following papers are enclosed:

- Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) concerning a filing under 35 U.S.C. 371.
- Preliminary Amendment.
- Declaration of Inventorship
- A cheque in the amount of \$500.00 with respect to the government filing fee is enclosed.
- PAYMENT OF THE CLAIM FEES IS BEING DEFERRED.
- The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to our Deposit Account No. 02-2095.
- Convention priority is requested based on United States Provisional Patent Application No. 60/444,684 filed on February 4, 2003 and No. 60/515,644 filed on October 31, 2003.

Respectfully submitted,

Patricia Power  
Registration No. 51,379

Manulife Corporate Park, 6733 Mississauga Road, Suite 600, Mississauga, Ontario L5N 6J5  
Tel: 905.812.3600 Fax: 905.814.0031 [www.bereskinparr.com](http://www.bereskinparr.com)

TORONTO MISSISSAUGA WATERLOO MONTREAL